November/December 2001

Editor:
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The Apothecary Bulletin

PHARMACY SERVICE & THERAPEUTICS COMMITTEES
US ARMY MEDDAC, FORT CARSON, COLORADO

FORMULARY CHANGES

The Pikes Peak Region Formulary Committee met on 6 December 2001 and the Evans Pharmacy and Therapeutics Committee met on 11 December 2001 with the following medications ***added*** to the Formulary:

+ desmopressin (*DDAVP*) 0.1mg & 0.2mg tablets
+ oxybutynin extended release (*Ditropan XL*) 5mg & 10mg tablets

The following medications were ***deleted*** from the Formulary:

- pancrealipase (*Ultrase*) capsules — were carried by the Air Force Academy; the only pancreatic enzyme preparations that will be available will be *Cotazym* and *Creon*

As some of you have heard, *Tequin* (gatifloxacin) was discussed at the Pikes Peak Region Formulary Meeting. Currently, the decision for formulary addition is **ON HOLD** until further discussion at the next meeting in January. *Levaquin* (levofloxacin) is on the **Basic Core Formulary** and will remain on Formulary. The DoD Formulary Committee also plans to review these agents in the near future.

As part of the ongoing drug class review process, the Pikes Peak Region Formulary Committee (with representatives from the Air Force Academy, Peterson AFB, and Evans) will conduct reviews as follows:

January 2002 = central nervous system
March 2002 = dermatologic/ophthalmologic

Pharmaceuticals submitted for Formulary consideration will be reviewed based on the above schedule. If a medication is a new entity, it may be considered earlier than the above schedule if submitted via a New Drug Request.

Providers desiring to have input into the drug class reviews are encouraged to contact one of the committee members: **LTC Edward Torkilson (Pharmacy), MAJ Robert Gray (Family Practice), and Dr. Garold Paul (Internal Medicine).** The next Formulary Committee Meetings are scheduled for 11 January 02 (Pikes Peak) and 12 February 02 (Evans' P&T). New Drug Requests must be received by the Chief, Pharmacy Service, no later than **28 December 01** (Pikes Peak) and **1 February 02** (Evans' P&T) to be considered at the next Formulary meetings.

SEASONS GREETINGS

The American Medical Association has changed its long-standing position on HIV testing for pregnant women, deciding to drop its policy that **mandated** HIV testing for all pregnant women. The organization still supports universal testing and counseling for pregnant women, suggesting "that there should be universal HIV testing of all pregnant women with notification of the right of refusal as a routine component of prenatal care..."

Q & A

What is the average cost to develop a new prescription drug?

see page 6

"You do not really understand something unless you can explain it to your grandmother."
— *Albert Einstein*

In this issue....

CHANGES TO *AMBIEN*

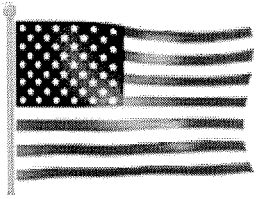
Effective 1 January 2002, a quantity limitation will be in effect for *Ambien* (zolpidem) 10mg at this facility. **Patients may be prescribed up to 10 tablets with no refills. The medication may NOT be renewed or reordered within 30 days of a previous prescription for *Ambien*.** Psychiatry Service is authorized to prescribe up to a 90 day supply with no refills. *Ambien* therapy for psychiatry patients will **NOT** exceed 180 days. Any therapy beyond 180 days with this medication will require completion of a New Drug Request and approval by the Chief of Psychiatry.

Ambien is indicated for the **SHORT-TERM** treatment of insomnia, not exceeding 7 to 10 days. While chemically unrelated to the benzodiazepines, pharmacologically this product works in a similar fashion. As such, abrupt discontinuation may lead to withdrawal symptoms if the patient has been routinely taking the medication for a prolonged period (greater than 2 weeks). The most common withdrawal symptoms are mild dysphoria and insomnia, which usually disappear within 2 to 3 days of discontinuing the medication.

These restrictions were approved at the December 2001 MEDDAC Pharmacy and Therapeutics meeting following the recommendations of the Pharmacy and Psychiatry Services.

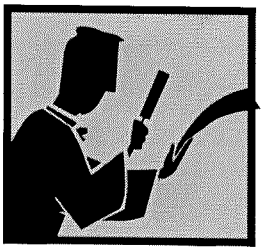
FUTURE PLAN FOR PPIs

A drug use evaluation was conducted by clinical pharmacy service on the switch to *Aciphex* (rabeprazole) from *Prilosec* (omeprazole) — see the Medication Use Review Committee report on page 6. Information was received by patient questionnaire and showed that most patients with mild to moderate GERD were able to tolerate the conversion (some with titration in the dose of *Aciphex*) but some patients with severe GERD were not being controlled with maximum dose of *Aciphex*. The Pharmacy Service in conjunction with GI Service is completing guidelines for the use of Proton Pump Inhibitors (PPIs) in GERD which will include recommendations for patients whose symptoms are not controlled with maximum dose of *Aciphex*. The guidelines will be sent to providers once completed and approved by the P&T Committee.



"Enjoy the peace your valor won.
Let independence be our boast,
Ever mindful what it cost;
Ever grateful for the prize,
Let its altar reach the skies!"
-- Joseph Hopkinson, 1770-1842

CHANGE TO NONFORMULARY PROCESS



DRUG WARNING — *INAPSINE*

The FDA has issued a **black box warning** regarding the use of *Inapsine* (droperidol). The FDA notes that this medication has been associated with QT segment prolongation and/or *torsades de pointes* and, in some cases, resulted in fatal cardiac arrhythmias. While *Inapsine* currently includes a warning about cases of sudden death at high doses (greater than 25mg) in patients at risk for cardiac arrhythmias, the FDA notes there have been cases of serious cardiac arrhythmias when used at, or below, the currently labeled dose range.

Physicians are encouraged to consider using alternative medications for patients at risk of cardiac arrhythmias, though they should be aware that potentially serious arrhythmias have occurred in patients with no known risk factors for QT prolongation.

HERB OF THE (every other) MONTH

Echinacea, commonly known as coneflower, has been touted as a natural immune system stimulator. Native to the central United States (found growing as a wildflower mostly in the prairies, the midwest states, and as far south as Texas) it was used in traditional medicine by Native American Indians for a variety of ailments including coughs, colds, insect stings, animal bites, and skin diseases and was quickly adopted by settlers. During the 1800s, claims for the curative properties of the plant ranged from a "blood purifier" to a treatment for dizziness and rattlesnake bites. During the early part of the 20th century, extracts of the plant were used as anti-infectives. With the discovery of modern antibiotics, the use of echinacea extracts fell out of favor. Echinacea is claimed to be useful as a wound healing agent for abrasions, burns, eczema, varicose ulcers of the leg and other skin wounds, and as a nonspecific immunostimulant for the supportive treatment of URIs and UTIs.

Echinacea dietary supplements are obtained from the dried rhizomes and roots of *Echinacea angustifolia* or *E. pallida* and from the fresh juice of the roots or above-ground parts of *E. purpurea.* Echinacea contains alkylamides, caffeic acid derivatives, polysaccharides, essential oils and other constituents, including polyacetylene flavonoids and glycoproteins. The concentration of the pharmacologic active constituents varies depending on the species and the plant part used. The mechanism of echinacea's inhibitory effects on microbial infections relates to its stimulation of the body's immune system rather than any significant direct antimicrobial action. A major part of its immunostimulation involves enhancement of macrophage phagocytosis and increased respiratory cellular activity and mobility of leukocytes.

Even with its popularity in Europe (over 2.4 million prescriptions were written for echinacea in Germany in 1994), few well-designed studies have been done. In the *Arch Fam Med* (Nov/Dec 1998), a blinded, placebo-controlled, randomized trial by German researchers in 289 patients with 2 species of echinacea or placebo for a 12-week period found no significant differences among the groups in the number, severity, or duration of URIs. In other studies, reductions in viral symptom severity and duration have been shown, but the study samples have been small.

Echinacea is recommended to be taken at the onset of viral symptoms and continued for 24 to 48 hours after resolution of symptoms. With prolonged use, echinacea may result in immune system overstimulation and eventual suppression. Dosages used vary depending upon the plant source used and the condition being treated. Dosage forms include capsules (containing powdered herb equivalent to 900mg to 1gm TID), tincture (0.75 to 1.5 ml or 15 to 30 drops orally 2 to 5 times per day), and expressed juice (6 to 9 ml orally daily). Doses are given 3 times a day for up to 10 days. Echinacea should not be used for longer than 8 weeks.

Echinacea appears to be well tolerated, relatively free of toxicity when given orally or topically. Mild allergic reactions can occur and serious reactions (dyspnea and anaphylaxis) have occurred in patients with asthma, allergic rhinitis, or allergies to plants of the daisy family. No drug interactions have been reported. Contraindications include patients with severe illnesses including HIV infection, collagen illness, leukosis, multiple sclerosis, and tuberculosis or other autoimmune disease. Avoid use in pregnancy or breast-feeding as the effects are unknown.

References: The Review of Natural Products, *Facts & Comparisons*
Herbs of Choice: The Therapeutic Use of Phytomedicinals, Varro Tyler, 1994

EVANS' ADR DEFINITION

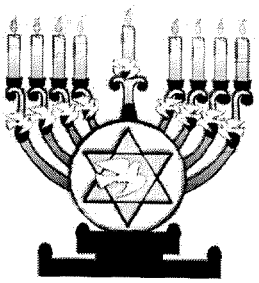
An adverse drug reaction (ADR) is any **unwanted or unintended effect (note: "unexpected" deleted from definition based on recommendation by JCAHO consultant)** of a drug following prescribed doses that (1) requires some sort of management including, but not limited to, discontinuation of the causative medication or treatment with another drug; (2) adversely impacts the outcome or progress of the patient's clinical condition; or (3) results in death, hospitalization, prolongation of hospital stay, transfer to a more intense level of care, or significant discomfort/distress to the patient.

HOW TO REPORT AN ADR

- Complete the **Adverse Drug Reaction Reporting Form** and return to the pharmacy. For forms, call the pharmacy at 526-7334.
- Use **CHCS e-mail and send to mail group "G.ADR"**. Please include the patient's name and SSN, date of occurrence, suspected drug, signs/symptoms of the event, and any changes/additions to therapy made.

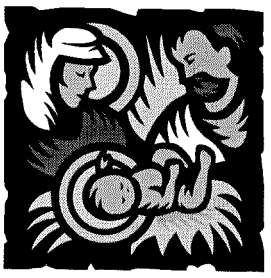
- Use **Website ADR Reporting** option located on the Evans Pharmacy Webpage. From the Evans Homepage, choose "Medical Clinics", then "Pharmacy", then search for "ADR" and follow the instructions. Reported ADRs are confidentially forwarded to the ADR Coordinator's e-mail.
- **Phone-in** the ADR to **52 I-ITCH** (524-4824). Please include the patient's name and SSN, date of occurrence, suspected drug, signs/symptoms of the event, and any changes/additions to therapy made. Make sure you include your name and extension in case more information or follow-up is needed.

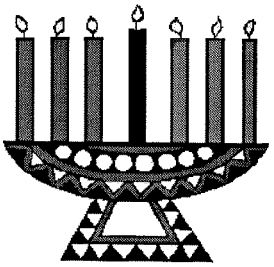
- **Phone-in** the ADR to the Inpatient Pharmacy at 524-4400 from 0600 to 2300 or call 526-7334 and leave a voice mail message with the information listed above. Make sure you include your name and extension in case more information or follow-up is needed.



Happy Hanukkah!

Merry Christmas!





Happy Kwanzaa!

History

- The celebration of the new year is the oldest of all holidays, first observed in ancient Babylon about 4000 years ago. In the years around 2000 BC, the Babylonian New Year began with the first New Moon (actually the first visible cresent) after the Vernal Equinox (the first day of spring). The Babylonian New Year celebration lasted for eleven days, each day having its own particular mode of celebration.
- The first rooftop celebration (a fireworks display) atop One Times Square took place in 1904 and was produced by *The New York Times* to inaugurate their new headquarters in Times Square and celebrate the renaming of Longacre Square to Times Square.
- The song *Auld Lang Syne* is sung at the stroke of midnight in almost every English-speaking country in the world to bring in the New Year. At least partially written by Robert Burns in the 1700's, it was first published in 1796 after Burns' death. Early variations of the song were sung prior to 1700 and inspired Burns to produce the modern rendition. *Auld Lang Syne* literally means "old long ago," or simply, "the good old days."

NEW DRUG APPROVALS/INDICATIONS

King Pharmaceuticals received FDA approval for its new drug application for *Tigan* (trimethobenzamide hydrochloride) 300mg capsules. It has been approved for the treatment of post-operative nausea and vomiting and for nausea associated with gastroenteritis.

Novartis Pharmaceuticals received FDA approval for *Elidel* (pimecrolimas) 1% cream, the first nonsteroidal prescription cream for mild to moderate atopic dermatitis in patients aged 2 years and older. *Elidel* is approved for the short-term and intermittent long-term treatment of mild to moderate eczema in patients who do not respond well to or may have side effects with conventional treatments.

Organon and Sanofi-Synthelabo received FDA approval for *Arixtra* (fondaparinux sodium), a synthetic compound and the first in a new class of antithrombotic agents that selectively inhibits Factor Xa. *Arixtra* is approved for the prophylaxis of DVT in patients undergoing hip fracture surgery, hip replacement surgery, and knee replacement surgery.

Cell Therapeutics, Inc. has been granted orphan drug designations for *Trisenox* (arsenic trioxide) injection for the treatment of both chronic myeloid and acute myelocytic leukemias.

Avelox IV formulary (moxifloxacin hydrochloride in sodium chloride for injection) received FDA approval for the treatment in adults of community-acquired pneumonia, acute bacterial sinusitis, acute bacterial exacerbations of chronic bronchitis, and uncomplicated skin and skin structure infections.

Endo Pharmaceuticals Holdings, Inc. received FDA approval to market *Percocet 7.5/325* and *10/325* (oxycodone/acetaminophen) tablets. The new reformulated strengths offer pain relief with reduced acetaminophen content as compared to previously available formulations.

Ortho-McNeil Pharmaceuticals, Inc. received FDA approval for the first birth control patch, *Ortho Evra*. This product delivers continuous levels of norelgestromin (the primary active metabolite of norgestimate) and ethinyl estradiol, with the patch worn for 1 week and replaced on the same day of the week for 3 consecutive weeks. The 4th week is "patch-free". A study published earlier this year in *JAMA* found that *Ortho Evra* was as effective in preventing pregnancy as the leading birth control pill. The patch can be worn on the buttocks, abdomen, upper torso (front and back, excluding the breasts), or upper outer arm.

" Peace is costly but it is worth the expense. "

-- Kikuyu of Kenya proverb

JANUARY is...

Cervical Health Awareness Month
National Birth Defects Prevention Month
National Glaucoma Awareness Month
National Volunteer Blood Donor Month

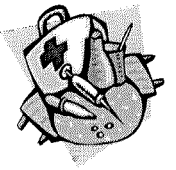
WEBSITES OF INTEREST

http://evans.amedd.army.mil – Evans' page
http://evans.amedd.army.mil/pharmnew/ — Evans' pharmacy website
http://www.pec.ha.osd.mil – DoD Pharmacoeconomic Center, Ft Sam Houston
http://www.cs.amedd.army.mil/qmo/pguide.htm – DoD/ VHA Practice Guidelines; current guidelines include Low Back Pain, Asthma, Diabetes, COPD, Hypertension, Hyperlipidemia, Tobacco Use Cessation, Major Depressive Disorder, Dysuria in Women

Birth Defects Websites

http://www.modimes.org/ — March of Dimes
http://www.cdc.gov/ncbddd/bd/ — CDC's Birth Defects website
http://vm.cfsan.fda.gov/~dms/wh-folic.html — FDA's Information Paper on Folic Acid
http://vm.cfsan.fda.gov/~dms/wh-preg.html — FDA's Information for Pregnant Women
http://www.rarediseases.org/cgi-bin/nord — National Organization for Rare Disorders, Inc
http://www.birthdefects.org/ — Birth Defects Research for Children, Inc.
http://www.nofas.org/ — National Organization on Fetal Alchol Syndrome
http://www.cleft.net/ — International Institute for Birth Defects
http://www.acog.org/ — The American College of Obstetricians and Gynecologists
http://www.aap.org/ — American Academy of Pediatrics
http://www.otispregnancy.org/index.html — Organization of Teratology Information Services

ADVERSE DRUG REACTION REPORT



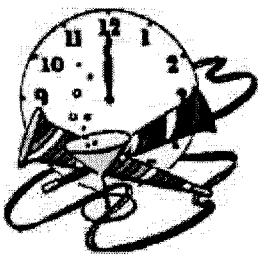
There were 38 adverse drug reactions (ADRs) documented for September (n=18) and October (n=20), of which 17 (45%) were reported **spontaneously** — 6 from pharmacy (inpatient/ outpatient/clinical); 4 from Preventative Medicine; 3 from Family Practice; 2 from Psychiatry; and 1 each from the ICU and Pediatrics. The most prevalent adverse events involved the anti-infective agents (n=9; 24%), the cardiovascular agents (n=6; 16%), and the psychotherapeutic agents (n=4; 11%). The anti-infective agents continue to be the top medication class involved in the reported adverse events. The rate of outpatient ADR reporting has remained consistent over the last year.

Two events were deemed moderate on the severity scale (mild, moderate, severe, fatal): a 76 year old male hospitalized for work-up of nausea found secondary to increased dose of *Humibid* and a 44 year old female hospitalized for pancreatitis secondary to *Maxzide*. Both patients recovered from the adverse events.

Two events were deemed preventable: a 44 year old male on *Coumadin* presented to the Emergency Department with gross hematuria with an INR of 10.8 (*Coumadin* dose held and patient instructed to follow-up with his civilian provider) and a 71 year old male on *Glucovance* (glyburide and metformin combination) who presented to the Emergency Department with hypoglycemia (changed back to previous therapy of metformin monotherapy and patient instructed to follow-up with his provider).

Thank you to all health care professionals who continue to report adverse events.

Happy New Year !!



May the best day of your past be the worst day of your future.
— Irish Toast

As you slide down the banisters of life, may the splinters never point the wrong way.
— Irish Toast

MEDICATION USE REVIEW COMMITTEE REPORT, RHONDA EUSTICE, PharmD

At their December meeting, the Medication Use Review (MUR) Committee, with representatives from the medical staff, nursing, clinical pharmacy, and nutrition, reviewed a drug use evaluation on the conversion to *Aciphex* from *Prilosec* which was completed by the clinical pharmacy member. The following is a summary of the review.

Prilosec to *Aciphex* Conversion — December 2001

Disease/Drug(s) Evaluated:
Aciphex for GERD

Purpose:
Prilosec was removed from the formulary and *Aciphex* was added in September 2001. A patient telephone questionnaire was conducted to evaluate the patient's perceptions of *Aciphex* effectiveness compared to *Prilosec.*

Patient Population/Sample Size:
A random sampling of 153 patients identified that were on *Prilosec* for GERD and had been switched to *Aciphex;* 43 patients (28%) were contacted.

Findings:
- 14% of patients stated that *Aciphex* works **better** than *Prilosec*
- 42% of patients stated that *Aciphex* works **just as well** as *Prilosec*
- 44% of patients stated that *Aciphex* **doesn't work as well** as *Prilosec*

For patients who reported *Aciphex* not as effective as *Prilosec*:
- *Prilosec* 20mg bid to *Aciphex* 20mg qd – 10%*
- *Prilosec* 20mg qd to *Aciphex* 20mg qd – 38%*
- *Prilosec* 20mg bid to *Aciphex* 20mg bid – 10%
- *Prilosec* 40mg qd to *Aciphex* 40mg qd – 21%
- *Prilosec* 20mg qd to *Aciphex* 40mg qd – 21%

**Aciphex* dose not maximized

Cost Data:
Prilosec 20mg (before taken off formulary) = $1.09/tablet
EACH pharmacy spending on *Prilosec* May 2001 through July 2001 = $256,367

Prilosec 20mg (now) = $2.02/tablet
Aciphex 20mg = $0.22/tablet

***** Cost Avoidance > $600,000 *****

Conclusions:
- *Prilosec* and *Aciphex* may not be equipotent milligram per milligram.
- *Aciphex* doses have not been maximized in some patients.
- Utilizing *Aciphex* instead of *Prilosec* will lead to a considerable cost avoidance.

Recommendations:
- **Maximize *Aciphex* dose (40mg qd) prior to submitting nonformulary request for *Prilosec***

Q & A

The Tufts Center for the Study of Drug Development reported that the average cost to develop a new prescription drug is:

$802 million

The last study done by the Tufts Center estimated the average cost of development to be $231 million (1987 dollars). Related Tufts Center research has found that it takes between 10 and 15 years to develop a new prescription medicine and win approval to market it in the Unites States.